Application No.: 10/526,690 12 Docket No.: 514862007400

Response to Non-Final Office Action of 6/17/2008

REMARKS

Claims 1-9 and 11 were pending in this application. Claims 2, 3, and 7 are currently amended. New claims 17-20 have been added. After entry of this amendment, claims 1-9, 11, and 17-20 are pending in this application. No new subject matter has been added.

Amendments

Amendments to the Specification

The specification has been amended to correct for a typographical error. The typographical error is the repeating of the variable "Y⁸" as recited in the specification as "V¹ to V⁴ are Y⁸ $_{m6}T_{o3}U$." The variable "Y⁸" was already in use as a substituent attached the "P" atom in the formula b) shown below:

b)

Therefore, this typographical error was corrected by the following amendment: " V^1 to V^4 are Y^8 $_{m6}T_{e3}U$ " and all subsequent " Y^n " variables were amended to " Y^{n+1} ." No new subject matter has been added.

Amendments to the Claims

Amendment and/or cancellation of certain claims is in no way an admission or acquiescence to the Examiner's rejection and is not to be construed as a dedication to the public any of the subject matter of the claims as previously presented. No new subject matter has been added.

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Claim 2 has been amended to correct for a typographical error in the "Y" variables in the same manner as was described under the section "Amendments to the Specification" presented above. Claim 2 has also been amended to clarify that: " V^1 to V^4 each have the formula $Y^9_{m6}T_{c3}U$ "; "Tol to To3 are the same or different in the above formula and are each independently selected from the group consisting of (CH₂)_n, CHCH, and CH₂CHCHCH₂"; "o1 to o3 are independently 0 or 1"; "U has a formula selected from the group consisting of R¹Y¹⁰_{m7}, CY¹¹Y¹²R², SY¹³Y¹⁴Y¹⁵R³, $PY^{16}Y^{17}Y^{18}R^4R^5,\,Y^{19}PY^{20}Y^{21}Y^{22}R^6R^7,\,CH_2NO_2,\,NHSO_2R^8,\,and\,\,NHCY^{23}Y^{24}R^9";\,"m1\,\,to\,\,m7\,\,are$ independently 0 or 1"; "Y1 to Y24 are the same or different and are each independently selected from the group consisting of NR¹⁰, NOR¹¹, O, and S"; and "R¹ to R¹¹ are the same or different and are each independently selected from the group consisting of" to clarify the scope of the claim. Claim 3 has been amended to recite that V¹ and V² "are the same or different in the above formula and are each independently selected from the group consisting of" to clarify the scope of the claim. Support for these clarifying amendments may be found throughout the specification, including the numerous embodiments having homologous and heterologous variable groups as claimed. Claim 7 has been amended to remove "preferably 5 to 18 atoms." New claims 17-20 have been added. Support for claim 17 may be found in the specification as originally filed and at least on page 10, lines 6-7. Support for claims 18-20 may be found in the specification as originally filed and at least on page 10, lines 31-34 to page 14, lines 1-7 No new subject matter has been added.

Examiner's Interview

Applicant thanks the Examiner for the courtesy of the telephonic interview of August 7, 2008 with Applicant's representative Brian Ho. Applicant noted that the disposition of claims as presented on Office Action Summary (claims 10 and 13-16 withdrawn) differed from the disposition provided in the Examiner's comments at page 2 (claims 10 and 12-16 withdrawn). The Examiner clarified that the proper listing of withdrawn claims is 10 and 12-16, as presented on page 2.

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Claim Rejections Under 35 USC § 112, Second Paragraph

Claim 2 is rejected under 35 USC § 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which Applicant regards as the

invention.

In the Office Action dated June 17, 2008, the Examiner noted that with respect to the set of

substituents R1 to R11 "the phrasing that uses the term 'are' says that they are all the same chemical

moiety." Claim 2 has been amended to recite that "R1" to R11 are each independently selected from

the group consisting of' to clarify that the R groups could be the same chemical moiety or different

chemical moieties. Therefore, Applicant believes the amended claim is no longer indefinite and

respectfully requests that this basis for rejection be withdrawn.

Claim 3 is rejected under 35 USC § 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which Applicant regards as the

invention.

In the Office Action dated June 17, 2008, the Examiner noted that with respect to the set of

substituents V1 and V2 "the phrasing that uses the term 'are' says that they are all the same chemical

moiety." Claim 3 has been amended to recite that V1 and V2 "are the same or different in the above

formula and are each independently selected from the group consisting of" to clarify that the V1 and

V² groups could be the same chemical moiety or different chemical moieties. Therefore, Applicant

believes the amended claim is no longer indefinite and respectfully requests that this basis for

rejection be withdrawn.

Claim 7 is rejected under 35 USC § 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which Applicant regards as the

invention.

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In the Office Action dated June 17, 2008, the Examiner noted that Claim 7 contained a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation. Claim 7 has been amended to remove the narrower limitation of "preferably 5 to 18 atoms" from the claim. New claim 17, which depends from claim 7, includes this narrower limitation of "5 to 18 atoms." Therefore, Applicant believes the amended claim is no longer indefinite and respectfully requests that this basis for rejection be withdrawn.

Claim Rejections Under 35 USC § 103

Persson et al. (U.S. Patent No.: 5,866,557) in view of Chudzik et al. (U.S. Pub No.: 2002/0032434)

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Persson *et al.* (U.S. Patent No.: 5,866,557) in view of Chudzik *et al.* (U.S. Pub No.: 2002/0032434).

The object of the coated stent as presently claimed is to prevent restenosis. Restenosis is a specific disease related to a re-narrowing or blockage of an artery at the same site where treatment, such as a balloon angioplasty or stent procedure has taken place. The condition occurs in patients who have undergone these procedures in up to half of all cases often within four to six months. Overgrowth of the normal tissue, similar to scar tissue occurs, which leads to tissue proliferation around the site where a balloon or stent has been or is located. The repair process leads to narrowing of the vessel walls which counteracts the beneficial effects introduced by the insertion of a balloon or a stent. The present application teaches testing protocols for compounds containing a high density, negatively charged domain of at least three vicinally oriented phosphorous-containing radicals to inhibit vascular smooth muscle cell proliferation which contributes to restenosis.

In the Office Action dated June 17, 2008, the Examiner noted that Persson *et al.* teach a collection of inositoltrisphosphate compounds that are used to treat inflammatory conditions. Inflammatory conditions are characterized by signs of pain, heat, redness and swelling and can appear at different places in the body most often in connection to chronic diseases such as rhinitis

and arthritis. In acute situations, after for example direct injury, inflammatory conditions can result in the above described signs, but these conditions are reversed within intervals of a few hours up to a few days. The Persson *et al.* reference teaches testing the esters of inositoltrisphosphate compounds for anti-inflammatory responses in rat hind-paw oedema models. The Chudzik *et al.* reference teaches bioactive agent release coatings on a stent, but do not teach how the bioactive agents are to selected or screened for specific therapeutic uses.

The combination of the references would not render obvious to one of skill in the art the claimed compound-coated stent for the prevention of restenosis. The teachings of the references or combinations of references do not lead one of skill in the art to select anti-inflammatory compounds to coat on a stent for an anti-restenosis application, and furthermore, the references do not teach one of skill in the art how to screen or test compounds coated on a stent for restenosis inhibition. Therefore, it would not be obvious to coat a stent with the compounds disclosed in the present application for the prevention of restenosis as presently claimed. Applicant respectfully requests that this basis for rejection be withdrawn.

Persson et al. in view of Chudzik et al., in view of Shvets (Russian Chemical Reviews 1974 43:488-502)

Claims 1-3 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Persson *et al.* in view of Chudzik *et al.* as applied to claims 1-9 above, and further in view of Shvets (Russian Chemical Reviews 1974 43:488-502).

For the reasons stated above, the coated stent of the present application are not obvious over the Persson *et al.* and Chudzik *et al.* references. The addition of the Shvets reference teaches the stereochemistry of myoinositol derivatives. Thus, the Shvets reference does not resolve the deficiencies of the Persson *et al.* and the Chudzik *et al.* references. Therefore, Applicant respectfully requests that this basis for rejection be withdrawn.

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Claim 20

New claim 20 is directed towards a coated stent that is coated with the compound D-myo-inositol-1,2,6-trisphosphate. Applicant notes that the compound D-myo-inositol-1,2,6-trisphosphate is not the same compound as the elected species D-3,4,5-tri-O-(phenylcarbamoyl)myo-inositol-1,2,6-trisphosphate.

None of the cited references teach the specific compound D-myo-inositol-1,2,6-trisphosphate of claim 20. Persson *et al.* disclose <u>esters</u> of inositoltrisphosphate compounds for the treatment of inflammatory conditions. The compound D-myo-inositol-1,2,6-trisphosphate is the free alcohol form of inositoltrisphophate; therefore, it is <u>not</u> an ester of inositoltrisphosphate. The Persson *et al.* reference recites that "the therapeutic profile of esters of inositoltrisphophates differs from the therapeutic profile of inositoltrisphophates in many important aspects." Persson *et al.*, column 2, lines 12-14. Therefore, neither the Persson *et al.* reference, the other cited references, or the combination of references would lead one of skill in the art to coat a stent with the inositoltrisphosphate compound D-myo-inositol-1,2,6-trisphosphate of claim 20.

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CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to <u>Deposit Account No.: 03-1952</u> referencing <u>Docket No.:</u> <u>514862007400</u>. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: September 15, 2008

Respectfully submitted,

Brian B. Ho

Registration No.: 60,199

MORRISON & FOERSTER LLP

425 Market Street

San Francisco, California 94105-2482

Telephone: 415.268.7624

Fax: 415.268.7522